Managing Your Patients’ Immune-Related Adverse Events (irAEs)

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Overview

- Overview of immune-related adverse events
  - Skin
    - Dermatitis
    - Oral Mucosa
  - Diarrhea/Colitis
  - Endocrinopathies
    - Thyroid disorders
    - Hypophysitis
    - Diabetes mellitus
    - Adrenalitis
  - Pneumonitis
  - Hepatitis
  - Nephritis
  - Other
- Relationship between irAE and treatment response
- Case studies
Skin

• Skin events most frequent irAE for both anti-CTLA-4 and anti-PD-1 blockade in melanoma patients
  • Anti-PD-1: Approx 40% in melanoma versus 17% in NSCLC\(^1\)
  • More common in anti-CTLA4 (50%) and combo (60%)\(^2\)
  • Grade 3/4 rash in less than 10%\(^2\)
• Includes vitiligo, rash, erythema
• Rarely Stevens-Johnson or Toxic epidermal necrosis

Dermatitis

• Symptoms
  • Rash
  • Itching
  • Fevers
  • Skin desquamation and sloughing of oral mucosa in severe cases (Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis)

• Work Up
  • Generally diagnosed based on appearance
  • Severe or treatment refractory cases may require biopsy

• Management
  Grade 1-2 managed with topical corticosteroids and oral antipruritic
    Eval for skin infections before applying topical steroid
  Grade 3-4 systemic steroid course
    Consider skin biopsy for histological classification
Oral Mucosa

• May include mucositis, gingivitis, and sicca (Sjogren) syndrome
• Approximately 5% of patients on checkpoint inhibitors have symptoms of dry mouth\(^1\)
  • More common in anti-PD1 agents\(^2\)
• Work-up:
  • Anti-nuclear antibodies (ANA)
  • Sjogren’s syndrome A & Sjogren’s syndrome B (SSA/SSB) screen
• Management:
  • Oral corticosteroid rinses
  • Pilocarpine chlorhydrate
  • Viscous lidocaine
  • Good oral hygiene
Diarrhea and/or Colitis

- Diarrhea and/or colitis is the most common and potentially most serious complication of anti-CTLA-4 therapy.
  - Some trials report up to 31% of patients experiencing some grade of diarrhea, with 6% experiencing severe colitis (Hodi, 2010).
  - Bowel perforation, sepsis, and death have been reported.
- Grade 3/4 colitis more common in CTLA-4 (7%) than PD-1 (1.8%)\(^1\)
  - Approximately 8% Grade 3/4 in combination therapy\(^2\)
- Median time to onset 6-8 weeks in CTLA-4 or CTLA-4/PD-1, longer in PD-1\(^1\)


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Diarrhea/Colitis

• Symptoms
  • Abdominal cramping, pain
  • Anorexia, dyspepsia
  • Diarrhea
  • Blood or mucous in stool
  • Leukocytosis
  • Serum electrolyte abnormalities
  • Possible to have colitis without diarrhea

• Work Up
  • Stool for c-diff, ova and parasite, blood
  • CT abdomen/pelvis with IV contrast to evaluate for colonic thickening and dilatation
  • Colonoscopy with biopsy
Diarrhea and/or Colitis

• Sigmoidoscopy/colonoscopy may be done if diagnosis is unclear
• Pathologic features resemble Crohn’s Disease
  • Mucosal erythema and ulcerations
  • Histologic patterns include lymphocytic and neutrophil inflammation with cryptitis and, in some cases, crypt abscesses and granuloma
Diarrhea/Colitis
Diarrhea and/or Colitis

• **Mild (Grade 1):** <4 stools/day above baseline
  • Bland diet, proton-pump inhibitors, loperamide ± diphenoxylate/atropine
  • May delay ipilimumab until symptoms improve

• **Moderate (Grade 2):** ≥4 to 6 stools/day
  • Consider colonoscopy; moderate-dose steroids: 0.5 mg/kg per day of methylprednisolone; increase dose if no improvement in 24 hours
  • Hold immunotherapy

• **Severe (Grade ≥3):** ≥7 stools/day
  • High-dose steroids: 1 mg/kg of methylprednisolone or equivalent
  • Discontinue immunotherapy
  • If unresolved within 1 week or symptoms worsen, consider infliximab (anti-TNF alpha)

• **Prevention with Budesonide (oral)** – Randomized phase II trial no benefit shown¹

• **Diarrhea/colitis with one checkpoint inhibitor does not prohibit use of another**²

¹ Weber J, et al., Clinical Cancer Research, 2009; ² Friedman et al, JAMA Oncology, 2016
Endocrinopathies

- Approximately 5-10% of patients treated with anti-CTLA-4 and anti PD-1/PD-L1 develop endocrinopathies¹
- Many endocrine disorders do not resolve—require life-long replacement
- May include:
  - Hypothyroid/Hyperthyroid
  - Hypophysitis
  - Adrenal insufficiency
  - Diabetes

¹ Michot et al, European Journal of Cancer, 2016
Thyroid Disorders

• Hypothyroidism most commonly seen with PD-1 (6%)\(^1\)
  • Primary hypothyroidism often preceded by transient hyperthyroidism\(^2\)
  • CTLA-4 approximately 5.6% of patients
  • Many studies did not distinguish between primary thyroid dysfunction (related to thyroid gland dysfunction) and secondary thyroid dysfunction (due to hypophysitis-related pituitary dysfunction)

• Evaluation:
  • High TSH, low/normal free T4 or T3 indicate primary hypothyroidism
  • Low/normal TSH, low free T4 suggests hypothyroidism secondary to pituitary
  • TPO antibodies, thyrotropin-binding inhibitory immunoglobulins

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Hypophysitis

- Inflammation of the pituitary resulting in low release of all or some of the following pituitary hormones\(^1\):
  - Adrenocorticotropic hormone (ACTH)
  - TSH
  - Follicle-stimulating hormone (FSH)
  - Luteinising hormone (LH)
  - Growth hormone (prolactin)

- Symptoms\(^1\):
  - Headache
  - Fatigue
  - Muscle weakness
  - Constipation
  - Cognitive difficulties (related to thyrotropin axis)
  - Erectile dysfunction/amenorrhea (gonadotropin axis, LH/FSH)
  - Orthostatic hypotension, hypoglycemia/hyponatremia (corticotrophin deficiency, ACTH)

Hypophysitis

Figure 2 | Normal pituitary tissues express ectopic CTLA4 protein. Binding to cytotoxic T-lymphocyte antigen 4 (CTLA4) autoantibodies or ipilimumab IgG1 to native CTLA4 proteins on normal pituitary tissue is thought to lead to activation of the classic complement pathway.

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Hypophysitis

• Work-up
  • Evaluation of pituitary gland hormones (ACTH, TSH, FSH, LH, prolactin, cortisol)
  • MRI brain with contrast (pituitary cuts)

Pre-Yervoy

Post-Yervoy
Diabetes Mellitus

- Rare occurrence with PD-1
- Patients generally present in DKA\(^1\)
- Work up should include testing for glutamic acid decarboxylase 65 (GAD65) antibodies
- Mechanism unclear\(^1\)
  - In one study, 2 of 5 patients presented with upregulation of CD8+ T cell response to a T1DM antigen
  - 3 of 5 patients were found to have GAD65 antibodies
- Treatment with insulin therapy


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Adrenalitis

• Primary adrenal insufficiency extremely rare but reported with CLTA4
• Adrenal gland enlargement can be seen on CT scans
• Work up:
  • ACTH
  • Cortisol
  • Cosyntropin stimulation test
• Management:
  Replacement with oral hydrocortisone

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Pneumonitis

- Occurs in approximately 1-2% of patients treated with PD-1 and/or CTLA4\textsuperscript{1,2}
- Time to onset 9-19 weeks (earlier with Nivolumab than Pembrolizumab)\textsuperscript{2}
- Symptoms:
  - Dry, unproductive cough
  - Dyspnea
  - Cyanosis (late)
  - Fatigue
- Differential Diagnosis:
  - Infection
  - Allergies
  - Cardiac causes (pericarditis)
- Late diagnosis may lead to chronic, irreversible lung disease\textsuperscript{2}

Pneumonitis

- **Work-Up:**
  - CXR and/or CT scan
    - Radiographic findings of ground-glass lesions and/or disseminated nodular infiltrates
  - Bronchoscopy
  - Pulmonary Function Testing (PFT)
  - Blood Gas

- **Treatment:**
  - Steroid therapy (guided by radiographic/symptomatic response)
  - Prophylactic antibiotic/antifungal therapy during high dose steroid
  - Mycophenolate mofetil, cyclophosphamide or infliximab in severe cases\(^1,2\)

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\(^1\) Eigentler et al, Cancer Treatment Reviews, 2016;  
\(^2\) Friedman et al, JAMA Oncology Review, 2016
Pneumonitis

CXR showing increased interstitial markings compared to baseline

Baseline

After 2 doses PD1/CTLA4
Hepatitis

• Incidence
  • Less common than colitis, seen in 2 to 9% of patients and at least 1 death has been reported on anti-CLTA-4 therapy alone
  • Incidence with anti-PD-1 closer to 0.5%
  • Hepatotoxicity appears worse when ipilimumab combined other drugs including dacarbazine and vemurafenib,
  • Combination therapy 15-18% overall and 6-8% grade 3-4

• Time to onset 8-12 weeks in single agent, sooner in combination

• Symptoms
  • Abdominal bloating or pain, dyspepsia, jaundice and nausea
  • Usually asymptomatic and diagnosed based on elevated LFT
Hepatitis

• Work Up
  • Hepatitis panel to evaluate for infectious cause
  • CT and/or ultrasound to evaluate for liver metastases or cholelithiasis
    • Patients with hepatitis may have mild hepatomegaly on imaging
  • Biopsy (if needed)
    • Diffuse T-cell infiltrate seen on pathology with diagnosis of hepatitis

• Treatment
  • High dose steroid (prednisone 1-2mg/kg)
  • Mycophenolate mofetil with steroid for severe cases
  • Infliximab is contraindicated due to hepatotoxic effects

Nephritis

- Seen in approximately 1% of patients on checkpoint inhibitor therapy\(^1\)
- Includes:
  - Interstitial nephritis with inflammatory cortical renal enlargement
  - Granulomatous nephritis
  - Glomerular lupus-like nephropathy
- Median time to onset variable (6-30 weeks)**
- Diagnosis to include CMP, urine studies, renal biopsy if needed
- Treatment with steroid

2. Eigentler et al, Cancer Treatment Reviews, 2016
Other irAE

- Pancreatic
  - Asymptomatic elevation in amylase/lipase
  - Pancreatitis
    - Radiographic findings of an inflamed pancreas, elevated amylase/lipase, clinical symptoms
- Clinical relevance of asymptomatic elevations remains unclear\(^1\)

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1. Friedman et al, JAMA Oncology Review, 2016
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Other irAE

• Neurologic\(^1\)
  • Less than 5% of patients receiving checkpoint inhibitors
• Includes:
  • Neuropathies
  • Aseptic meningitis
  • Temporal arteritis
  • Myastenia gravis
  • Guillain-Barre syndrome

• Treatment with steroid not universally effective
  • May need IVIG

1. Friedman et al, JAMA Oncology Review, 2016

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Other irAE

- Polyarthritis/Arthralgia\(^1\)
  - Seen in approximately 5% of patients
  - Reported cases erythematous lupus or polymyalgia rheumatic
  - ANA and anti-cyclic citrullinated peptide to detect auto-immune condition
  - Low dose oral steroid to control joint manifestations

- Hematologic toxicity
  - Anemia described in <5% CTLA4 and <10% PD1\(^2\)
  - Red cell aplasia, autoimmune neutropenia, pancytopenia, acquired hemophilia A also reported\(^1\)
  - Work up to include peripheral smear, reticulocyte count, Coomb’s test, hemolysis assays and bone marrow biopsy\(^1\)

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Other irAE

Fulminant Myocarditis with Combination Immune Checkpoint Blockade

- 2 patients with melanoma who developed fatal myocarditis after treatment with ipilimumab and nivolumab
  - Myositis with rhabdomyolysis
  - Early progressive and refractory cardiac electrical instability
- Myocarditis with robust presence of T-cell and macrophage infiltrates
- Pharmacovigilance studies showing that myocarditis occurred in 0.27% of patients treated with a combination of ipilimumab and nivolumab
Cerebral vasculitis mimicking intracranial metastatic progression of lung cancer during PD-1 blockade

- Metastatic adenocarcinoma patient treated with PD-1
- Developed cerebral lesions while having disease stabilization of extracranial metastases
- Lesion progressed despite stereotactic irradiation
- Resected specimen showed cerebral vasculitis, no cancer
- +ANA and anti-vascular endothelial antibodies in serum
Onset and Resolution

A. Time to onset (median, range)

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>n=30 (rash only); n=171; n=15 (data for +3/4 AE only)</th>
<th>n=23; n=78; n=16 (colitis only)</th>
<th>n=30; n=40; n=122</th>
<th>n=8; n=9; n=4</th>
<th>n=3; n=29; n=8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>Skin (n=30)</td>
<td>4.3</td>
<td>8.1</td>
<td>22.7</td>
<td>11.6</td>
</tr>
<tr>
<td>GI</td>
<td>GI (n=23)</td>
<td>6.3</td>
<td>5.6</td>
<td>18.1</td>
<td>8.7</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Pulmonary (n=13)</td>
<td>17.8</td>
<td>8.1</td>
<td>21.2</td>
<td>10.5</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Endocrine (n=12)</td>
<td>12.8</td>
<td>4.5</td>
<td>4.5</td>
<td>29.6</td>
</tr>
<tr>
<td>Renal</td>
<td>Renal (n=8)</td>
<td>10.5</td>
<td>6.1</td>
<td>29.6</td>
<td>25.1</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Hepatic (n=3)</td>
<td>4.1</td>
<td></td>
<td>3.1</td>
<td></td>
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</table>

B. Time to resolution (median, range)

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>n=24</th>
<th>n=19</th>
<th>n=13</th>
<th>n=6</th>
<th>n=7</th>
<th>n=3</th>
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</thead>
<tbody>
<tr>
<td>Skin</td>
<td>Skin</td>
<td>5.7</td>
<td>0.1-46.9+</td>
<td>20.6</td>
<td>0.4-17.6+</td>
<td>5.9</td>
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<tr>
<td>GI</td>
<td>GI</td>
<td>2.0</td>
<td>0.1-31.0+</td>
<td>2.0</td>
<td>0.6-13.4+</td>
<td>2.0</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Pulmonary</td>
<td>2.0</td>
<td>0.1-31.0+</td>
<td>2.0</td>
<td>0.6-13.4+</td>
<td>2.0</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Endocrine</td>
<td>2.0</td>
<td>0.1-31.0+</td>
<td>2.0</td>
<td>0.6-13.4+</td>
<td>2.0</td>
</tr>
<tr>
<td>Renal</td>
<td>Renal</td>
<td>5.9</td>
<td>0.7-37.6+</td>
<td>20.6</td>
<td>0.4-17.6+</td>
<td>5.9</td>
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<tr>
<td>Hepatic</td>
<td>Hepatic</td>
<td>2.0</td>
<td>0.1-31.0+</td>
<td>2.0</td>
<td>0.6-13.4+</td>
<td>2.0</td>
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</tbody>
</table>

C. Patterns of resolution (percent)

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>CA209017/063 sq NSCLC</th>
<th>CA209037/066 Melanoma</th>
<th>P001/002 Melanoma</th>
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</thead>
<tbody>
<tr>
<td>Skin</td>
<td>83%</td>
<td>46%</td>
<td>73%</td>
</tr>
<tr>
<td>GI</td>
<td>83%</td>
<td>91%</td>
<td>94%</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>100%</td>
<td>50%</td>
<td>65%</td>
</tr>
<tr>
<td>Endocrine</td>
<td>50%</td>
<td>44%</td>
<td>12-79%*</td>
</tr>
<tr>
<td>Renal</td>
<td>71%</td>
<td>61%</td>
<td>100%</td>
</tr>
<tr>
<td>Hepatic</td>
<td>67%</td>
<td>46%</td>
<td>75%</td>
</tr>
</tbody>
</table>

* Range: from 12 % (Hypothyroidism) until 79% (Hyperthyroidism)
## Serum Auto-Antibodies

Serum auto-antibody assays with potential value for identifying IRAEs.

<table>
<thead>
<tr>
<th>Immune-related organ involved</th>
<th>Antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastro-intestinal</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Antinuclear antibodies (ANAs)</td>
</tr>
<tr>
<td></td>
<td>Anti-smooth muscle, anti-liver kidney microsomal antibody type 1, anti-liver cytosol type 1</td>
</tr>
<tr>
<td>Lung</td>
<td>Antinuclear antibodies (ANAs)</td>
</tr>
<tr>
<td></td>
<td>Rheumatoid factor</td>
</tr>
<tr>
<td></td>
<td>Anti-centromere</td>
</tr>
<tr>
<td></td>
<td>Extractable nuclear antigens (ENA): anti-Sm, anti-RNP; anti-Ro (SSA), anti-La (SSB); anti-Scl70, anti-Jo</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Thyroid</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Anti-GAD, anti-insulin, anti-carbonic anhydrase</td>
</tr>
<tr>
<td>Addison’s disease</td>
<td>Anti-21 hydroxylase</td>
</tr>
<tr>
<td>Hypophysitis</td>
<td>Anti-pituitary</td>
</tr>
<tr>
<td>Skin</td>
<td>None</td>
</tr>
<tr>
<td>Poliarthritis</td>
<td>Antinuclear antibodies (ANAs)</td>
</tr>
<tr>
<td></td>
<td>Anti-ENA: Anti-SSA, SSB, Sm</td>
</tr>
<tr>
<td></td>
<td>Anti-CCP, complement fractions C3 C4 CH50</td>
</tr>
<tr>
<td>Renal</td>
<td>Antinuclear antibodies (ANAs)</td>
</tr>
<tr>
<td></td>
<td>Complement fractions C3 C4 CH50</td>
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<tr>
<td></td>
<td>Anti-neutrophil cytoplasmic (ANCA)</td>
</tr>
<tr>
<td>Haematologic syndromes</td>
<td>Antinuclear antibodies (ANAs)</td>
</tr>
<tr>
<td></td>
<td>Coombs’ erythrocyte test</td>
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</tbody>
</table>

IRAEs = immune-related adverse events; CCP = cyclic citrullinated peptide; GAD = Glutamate decarboxylase; RNP = ribonucleoprotein; Sm = Small nuclear ribonucleoprotein; SSA = Sjogren’s syndrome-related antigen A; Scl = Scleroderma systemic; SSB = Sjogren’s syndrome-related antigen B; TPO = Thyroid peroxidase.

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irAE and Overall Survival

- Cutaneous irAE associated with improved outcomes in melanoma
- Moffitt Cancer Center study of 148 patients treated with nivolumab plus peptide vaccine or nivolumab alone
  - Statistically significant OS benefit with rash (P=0.0001; HR 0.423)
  - Statistically significant OS benefit with vitiligo (P=0.012; HR 0.184)
    - Rash and vitiligo correlated with OS differences in metastatic disease (P=0.0004 and P=0.028, respectively)
  - No significant survival differences seen with endocrinopathies, colitis or pneumonitis in this study

![Table 3: Effect of irAE development on survival, using time-dependent Cox regression analyses](image)

irAE and Overall Survival

- Hypophysitis may be associated with improved outcomes
  - Massachusetts General Hospital study of 154 patients treated with Ipilimumab
    - Median survival in patients with ipi-induced hypophysitis was 19.4 vs 8.8 months (P=0.05)

Do Steroids Decrease Effectiveness? Probably Not

- Retrospective study of patients with melanoma treated with ipilimumab
- N = 298
- irAE, any grade: 254 (85%)
- Steroid therapy required: 103 (35%)
- Time to Treatment Failure, Overall Survival: the same in both groups

Case Study #1
Patient DC

65 y/o female with Stage IVa (T2N2bM0) squamous cell carcinoma of the right tonsil

Oncologic history:

10/20/2013: R-sided tonsillectomy w/ pathology revealing poorly differentiated SCCa, HPV/P16+

11/1/2013: PET/CT FDG uptake in right tonsillar pillar (SUV 5.4), no cervical lymphadenopathy noted

11/2013: Right pharyngectomy and right lymph node dissection

Post-op tx w/ XRT and weekly cisplatin, developed tinnitus and then on week 3 switched to carboplatin; tinnitus ultimately resolved

3/11/2016: CT chest revealing 2 separate round nodules; 1 in right lower lobe (1.8x1.5cm) and another in left upper lobe (1.3x1.1cm)

3/14/2016: PET/CT revealing left upper lobe and right lower lobe pulmonary nodules with intense associated increased uptake consistent with pulmonary metastatic disease, new since prior PET/CT; no evidence of local recurrence in pharyngeal soft tissues

3/17/2016: CT-guided biopsy of new PET positive lung nodules -> path: SCCa

4/29/16-10/4/16: Started EXTREME with 5FU, Carbo and Cetuximab, 5FU stopped at cycle 2, Carbo stopped at cycle 7

11/14/16: Started on Pembrolizumab
Patient DC

Right lung nodule prior to initiation of pembrolizumab (10/13/16)
Patient DC

- Tolerating therapy well through the first three cycles
  - Mild joint pains controlled with 10mg prednisone
- 1/20/17 presents for C4D1 pembrolizumab
  - Complains of headaches, dizziness, fatigue
  - Looks unwell
  - Obtain MRI brain with pituitary cuts
  - Check thyroid function

<table>
<thead>
<tr>
<th></th>
<th>ACTH (pg/ml)</th>
<th>TSH (ml/UL)</th>
<th>T4 (ng/dL)</th>
</tr>
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<tbody>
<tr>
<td>Pre</td>
<td>30</td>
<td>1.3</td>
<td>1.1</td>
</tr>
<tr>
<td>Post</td>
<td>4</td>
<td>0.39</td>
<td>0.3</td>
</tr>
<tr>
<td>Reference</td>
<td>10-50</td>
<td>0.5-5.5</td>
<td>0.89-1.76</td>
</tr>
</tbody>
</table>
Patient DC

Pre-treatment

Prior to cycle 4
Patient DC

- Grade 2 adrenal insufficiency due to hypophysitis
  - Initiated on hydrocortisone 20mg QAM, 10mg QPM
- Grade 2 hypothyroidism due to hypophysitis
  - Initiated on levothyroxine 100mcg PO daily
- OK to continue pembrolizumab
Patient DC

• Presents 4/14/17 for C8 Pembrolizumab
  • Lethargic, tachycardic
  • Complains of severe thirst and frequent urination
  • Random glucose 524
  • Admit for emergent management and work-up
Patient DC

- Glutamic acid decarboxylase 65 (GAD65) antibodies positive
- Diagnosed with new onset DM1 secondary to pembrolizumab
- Pembrolizumab discontinued
- Patient initiated on life-long insulin therapy
Patient DC

Baseline

After 7 Cycles of Pembrolizumab
Case Study #2
Patient MM

- 78 year old male with IV melanoma with widely metastatic melanoma diagnosed 6/2016
- PMH: Hypertension, Hypercholesterolemia, Asthma, Vitiligo
- PSH: Hernia repair, back surgery
- Medications: lisinopril, lorazepam, simvastatin, oxycodone
Patient MM

- Baseline PET scan showing widely metabolic disease
Patient MM

- Initiated on Ipilimumab (3mg/kg) + Nivolumab (1mg/kg)
  - C1D1 7/1/16
  - C2D1 7/22/16
  - C3D1 8/19/16
- 8/27/16 patient presents to outside hospital complaining of fever, cough and shortness of breath
  - VS: BP 125/86, HR 90, RR 22, O2 90%, Temp 100.1
  - CXR: Read as RML pneumonia
  - Patient initiated on Augmentin 875mg/125mg Q12
Patient MM

Baseline

8/27/16
Patient MM

• 8/30/16 patient presents to clinic with continued low grade fever, cough and diarrhea since 8/29/16
• Denies sick contacts, dietary changes
• Approximately 8 loose bowel movements per day (baseline 1 BM daily)
• No relief with imodium
• Cough making it difficult to sleep at night
Patient MM: Differential Diagnoses

• Grade 3 Diarrhea Differential Diagnoses:
  • Infectious diarrhea (including c-diff)
  • Antibiotic associated diarrhea
  • Colitis secondary to immunotherapy

• Grade 3 Cough v Pneumonitis Differential Diagnoses:
  • Infectious
  • Inflammatory
  • Irritation
Patient MM: Imaging

Chest CT scan:

Abdominal CT scan:
Patient MM: irAE Diagnoses

• Grade 3 Colitis and Grade 3 Pneumonitis
  • Initiate steroid at 1mg/kg of solumedrol or equivalent
  • Recommend IV steroid initially with colitis symptoms due to gut absorption issues
  • Taper slowly (one month)
  • Consider antibiotic prophylaxis during high dose steroid
  • Discontinue immunotherapy
Patient MM

Baseline

After three doses
QUESTIONS
Thank you for participating in the ACCC/OSSN Webinar. Presentation slides and archived recording will be available at accc-cancer.org.